

RECEIVED

NOV 22 2006

File Information Unit

PTO/SB/68 (11-04)

Approved for use through 7/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

Bring completed form to:

File Information Unit, Room 2E04

2900 Crystal Drive

Arlington, VA 22202-3514

Telephone: (703) 308-2733

In re Application of

Weiss et al.

Application Number

08/338730

Filed

11/14/94

Paper No. *23*

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is not within the file jacket of a pending Continued Prosecution Application (CPA) (37 CFR 1.53(d)) and which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____,

United States Patent Number *5750376*, column *1*, line, *1* or

WIPO Pub. No. _____, page _____, line _____.

Related Information About Access to Applications Maintained in the Image File Wrapper System (IFW) and Access to Pending Applications in General

A member of the public, acting without a power to inspect, cannot order applications maintained in the IFW system through the FIU. If the member of the public is entitled to a copy of the application file, then the file is made available through the Public Patent Application Information Retrieval system (Public PAIR) on the USPTO internet web site (www.uspto.gov). Terminals that allow access to Public PAIR are available in the Public Search Room. The member of the public may also be entitled to obtain a copy of all or part of the application file upon payment of the appropriate fee. Such copies must be purchased through the Office of Public Records upon payment of the appropriate fee (37 CFR 1.19(b)).

For published applications that are still pending, a member of the public may obtain a copy of:

the file contents; the pending application as originally filed; or any document in the file of the pending application.

For unpublished applications that are still pending:

- (1) If the benefit of the pending application is claimed under 35 U.S.C. 119(e), 120, 121, or 365 in another application that has: (a) issued as a U.S. patent, or (b) published as a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of: the file contents; the pending application as originally filed; or any document in the file of the pending application.
- (2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of the pending application as originally filed.

Signature

Date

Typed or printed name

Registration Number, if applicable

Telephone Number

RECEIVED

NOV 22 2006

File Information Unit

FOR PTO USE ONLY

Approved by:

(initials)

Unit:

This collection of information is required by 37 CFR 1.11 and 1.14. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. BRING TO: File Information Unit, Room 2E04, 2900 Crystal Drive, Arlington, Virginia.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



US005750376A

United States Patent [19]

Weiss et al.

[11] **Patent Number:** 5,750,376[45] **Date of Patent:** May 12, 1998[54] **IN VITRO GROWTH AND PROLIFERATION OF GENETICALLY MODIFIED MULTIPOTENT NEURAL STEM CELLS AND THEIR PROGENY**[75] **Inventors:** Samuel Weiss; Brent Reynolds, both of Alberta, Canada; Joseph P. Hammang; E. Edward Baetge, both of Barrington, R.I.[73] **Assignee:** NeuroSpheres Holdings Ltd., Calgary, Canada[21] **Appl. No.:** 483,122[22] **Filed:** Jun. 7, 1995**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 270,412, Jul. 5, 1994, abandoned, Ser. No. 385,404, Feb. 7, 1995, abandoned, Ser. No. 359,945, Dec. 20, 1994, abandoned, Ser. No. 376,062, Jan. 20, 1995, abandoned, Ser. No. 149,508, Nov. 9, 1993, abandoned, Ser. No. 311,099, Sep. 23, 1994, abandoned, and Ser. No. 338,730, Nov. 14, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 385,404, Feb. 7, 1995, abandoned, is a continuation of Ser. No. 961,813, Oct. 16, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 359,945, Dec. 20, 1994, abandoned, is a continuation of Ser. No. 221,655, Apr. 1, 1994, abandoned, which is a continuation of Ser. No. 967,622, Oct. 28, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 376,062, Jan. 20, 1995, abandoned, is a continuation of Ser. No. 10,829, Jan. 29, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 270,412, Jul. 5, 1994, abandoned, Ser. No. 149,508, Nov. 9, 1993, abandoned, and Ser. No. 311,099, Sep. 23, 1994, abandoned, each is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned.

[51] **Int. Cl.**⁶ C12N 5/00; C12N 5/08; C12N 5/10; C12P 1/00

[52] **U.S. Cl.** 435/69.52; 435/69.1; 435/172.3; 435/325; 435/368; 435/377; 435/384; 435/392; 435/395

[58] **Field of Search** 435/240.2, 172.3, 435/69.1, 69.52, 325, 368, 377, 384, 392, 395

[56] **References Cited****U.S. PATENT DOCUMENTS**

4,753,635	6/1988	Sagen et al.	604/49
4,980,174	12/1990	Sagen et al.	424/563
5,082,670	1/1992	Gage	424/520
5,175,103	12/1992	Lee et al.	435/172.3
5,411,883	5/1995	Boss et al.	435/240.2
5,612,211	3/1997	Wilson et al.	435/378

FOREIGN PATENT DOCUMENTS

0 233 838	8/1987	European Pat. Off.
89/03872	5/1989	WIPO
90/06757	6/1990	WIPO
91/02003	2/1991	WIPO
91/09936	7/1991	WIPO
91/17242	11/1991	WIPO
93/01275	1/1993	WIPO

93/09802 5/1993 WIPO
94/03199 2/1994 WIPO

OTHER PUBLICATIONS

Almazan et al., "Epidermal Growth Factor and Bovine Growth Hormone Stimulate Differentiation and Myelination of Brain Cell Aggregates in Culture," *Developmental Brain Research*, 21:257-264 (1985).

Anchan et al., "Trophic Factors Influence Proliferation of Germinal Neuroepithelial Cells of the Retina," *J. Cell Biol.*, 109:58a, Abstract No. 308 (1989).

Anchan et al., "EGF and TGF- α Stimulate Retinal Neuroepithelial Cell Proliferation in Vitro," *Neuron*, 6(6):923-936 (1991).

Bayer et al., "Neuron production in the Hippocampus and olfactory bulb of the adult rat Brain: addition or replacement?", *Annals NY Acad. Sci.* 457:163-172 (1985).

Björklund et al., "Neural Grafting in Animal Models of Neurodegenerative Diseases," *Ann. New York Acad. Sci.*, 457:53-81 (1985).

Bouvier et al., "Basic Fibroblast Growth Factor (bFGF) Promotes the Survival and Proliferation of Mesencephalic Neuronal Precursors in Vitro," *Society for Neuroscience Abstracts*, vol. 18, Abstract No.: 403.7 (1992).

Boyles et al., "Accumulation of Apolipoproteins in the Regenerating and Remyelinating Mammalian Peripheral Nerve," *J. Biol. Chem.*, 265(29):17805-17815 (1990).

Calof et al., "Analysis of Neurogenesis in a Mammalian Neuroepithelium: Proliferation and Differentiation of an Olfactory Neuron Precursor in Vitro," *Neuron*, 3:115-127 (1989).

(List continued on next page.)

Primary Examiner—George C. Elliott
Assistant Examiner—Johnny F. Railey, II
Attorney, Agent, or Firm—Flehr Hohbach Test Albritton & Herbert; David J. Brezner; Jan P. Brunelle

[57] **ABSTRACT**

A method for producing genetically modified neural cells comprises culturing cells derived from embryonic, juvenile, or adult mammalian neural tissue with one or more growth factors that induce multipotent neural stem cells to proliferate and produce multipotent neural stem cell progeny which include more daughter multipotent neural stem cells and undifferentiated progeny that are capable of differentiating into neurons, astrocytes, and oligodendrocytes. The proliferating neural cells can be transfected with exogenous DNA to produce genetically modified neural stem cell progeny. The genetic modification can be for the production of biologically useful proteins such as growth factor products, growth factor receptors, neurotransmitters, neurotransmitter receptors, neuropeptides and neurotransmitter synthesizing genes. The multipotent neural stem cell progeny can be continuously passaged and proliferation reinitiated in the presence of growth factors to result in an unlimited supply of neural cells for transplantation and other purposes. Culture conditions can be provided that induce the genetically modified multipotent neural stem cell progeny to differentiate into neurons, astrocytes, and oligodendrocytes in vitro.

40 Claims, 3 Drawing Sheets